ABSTRACT

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Radiolabelled receptor-specific peptides from the group of gastrin and bombesin derivatives are currently intensively researched substances in terms of targeting certain tumors. The main limit in their application is the intense renal accumulation and subsequent radiotoxicity. The aim of this experimental study was to determine and then compare the renal uptake of DOTA-bombesin and one of the gastrin derivatives - DOTA-sargastrin labeled with indium-111 and lutetium-177. Moreover, the other goal of this study was to assess the potential role of megalin system in the active endocytosis in the renal accumulation of these substances. Isolated rat kidney cells obtained by the collagenase perfusion method were used as an experimental model. The uptake of studied radiopeptides was further compared with the degree of accumulation of selected comparators with different renal accumulation (^{99m}Tc-DTPA, ^{99m}Tc-MAG3). The results of accumulation studies showed that the accumulation of the labeled derivatives of DOTA-sargastrin in rat kidney cells was relatively higher than of the derivatives of DOTA-bombesin. In addition, the degree of accumulation of ^{111}In-DOTA-sargastrin was significantly higher than of ^{177}Lu-DOTA-sargastrin. The accumulation of all studied radiopeptides was lower than that of ^{99m}Tc-MAG3 and lower or comparable with the accumulation of ^{99m}Tc-DTPA. When incubated at lower temperatures (2-4°C), which inhibits active transport mechanisms, a significant reduction in the accumulation in cells of ^{111}In-DOTA-sargastrin was observed. The effect of reduced uptake was absent in the case of ^{111}Lu-DOTA-bombesin and ^{177}Lu-DOTA-sargastrin. The addition of aprotinin, an inhibitor of the megalin system, did not lead to a reduced accumulation. Based on these inconsistent results it was not possible to make a definite conclusion about the role of active transport and megalin endocytary system in the accumulation of studied radiopeptides in renal cells.